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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,137	02/17/2004	Tamara Minko	744-53	2173
23869	7590	04/18/2007	EXAMINER	
HOFFMANN & BARON, LLP			FETTEROLF, BRANDON J	
6900 JERICHO TURNPIKE				
SYOSSET, NY 11791			ART UNIT	PAPER NUMBER
				1642
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE		DELIVERY MODE
3 MONTHS		04/18/2007		PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/780,137	MINKO ET AL.
	Examiner Brandon J. Fetterolf, PhD	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 23 February 2007.

2a) This action is **FINAL**.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 5,10,15 and 16 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 5, 10 and 15-16 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:
 

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____.	6) <input type="checkbox"/> Other: _____.

## DETAILED ACTION

### ***Response to Amendment***

The Amendment filed on 2/23/2007 in response to the previous Final Office Action (10/18/2006) is acknowledged and has been entered. The Finality of the previous Office Action has been withdrawn in view of the new rejections.

Claims 5, 10 and 15-16 are currently pending and under consideration.

### **New Rejections Upon further Considerations:**

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 5, 10 and 15-16 rejected under 35 U.S.C. 103(a) as being unpatentable over Trouet et al. (WO 01/91798, 2001, *of record*) in view of Chatzistamou et al. (Clinical Cancer Research 2000; 6: 4158-4165, *of record*).

Trouet et al. teach a prodrug for treating cancer comprising a biologically active entity linked to a masking moiety via a linking moiety (abstract). With regards to the biologically active entity, the WO document teaches (page 60, claim 51 of the WO document) that the biologically active entity includes, but is not limited to, BH3 peptides and anticancer agents such as anthracyclines,

doxorubicin and camptothecins. With regards to the linking group, Trouet et al. teach (page 2, lines 17-23) that the linking moieties are preferably peptides having the amino acid sequence of  $(\text{Leu})_y(\text{Ala-Leu})_x\text{Ala-Leu}$  and  $(\text{Leu})_y(\text{Ala-Leu})_x\text{Ala-Phe}$ , where  $y$  is 0 or 1 and  $x$  is 1, 2, or 3. With regards to the masking moiety, the WO document teaches (page 5, lines 21-33, page 15, lines 16-35 and page 32, lines 14 +) that the masking moiety may have biological activity such that prodrug is a dual prodrug and further, comprise large molecular weight biologically inert molecules such as PEG or HPMA. Trout et al. further teach (page 6, lines 18-24) a method of treating cancer comprising administering the prodrug to an animal in an effective amount to shrink or eradicate the tumor. Furthermore, the WO document teaches (page 35, lines 24+) a method of making the prodrug comprising condensing the masking moiety and biological entity with the linking moiety. Although Trouet et al. does not specifically teach that the linking moiety is a scaffold, the claimed limitation does not appear to result in a manipulative difference between the prior art because independent claim 10 and 16 recite that the scaffold is a peptide.

Trouet et al. do not explicitly teach that the prodrug further comprises LHRH.

Chatzistamou et al. teach an effective treatment of metastatic MDA-MB-435 human estrogen breast carcinomas which utilizes LH-RH analogues as targeted carriers for chemotherapeutics agents such as doxorubicin (Title and Abstract). Specifically, the references teaches that targeted chemotherapy is based on the concept of linking cytotoxic radicals to a carrier, which is able to recognize cancer cells, wherein selective accumulation of the chemotherapeutic agent can be achieved in the tumor while sparing the healthy tissues from exposure (page 4158, 2<sup>nd</sup> column, 2<sup>nd</sup> full paragraph). Moreover, Chatzistamou et al. teaches that the LH-RH analogues specifically target LH-RH receptors present on a variety of human tumors (page 4158, 2<sup>nd</sup> column, 3<sup>rd</sup> full paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the reference so as to modify the dual prodrug taught by Trouet et al. to include LHRH in view of the teachings of Chatzistamou et al.. One would have been motivated to do so because Chatzistamou et al. teaches that the targeted chemotherapy is based on the concept that by linking cytotoxic radicals to a carrier, which is able to recognize cancer cells, a selective accumulation of the chemotherapeutic agent can be achieved in the tumor while sparing the healthy tissues from exposure. Thus, one of ordinary skill in the art would have a

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reasonable expectation of success that by modifying the dual prodrug taught by Trouet et al. to include LHRH in view of the teachings of Chatzistamou et al, one would achieve a drug delivery complex which specifically targets tumors having LH-RH receptors and treating said tumors.

Therefore, NO claim is allowed

**All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD  
Patent Examiner  
Art Unit 1642

BF



  
SHANON FOLEY  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600